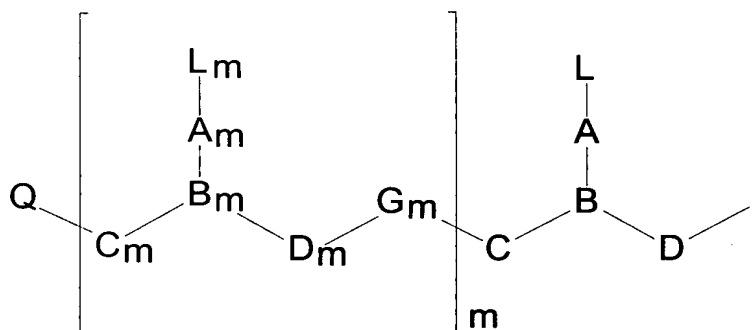


Listing of Claims:

53. (currently amended) A peptide nucleic acid ~~conjugate~~ of the formula:



~~R⁶ and R⁷ independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C₂-C₆) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆) alkoxy, (C₁-C₆) alkylthio, a conjugate, NR³R⁴, SR⁵ or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system;~~

DOCKET NO.: ISIS-1158
 Application No.: 08/319,411
 Office Action Dated: January 22, 2004

wherein R^5 is ~~hydrogen, a conjugate, (C₁-C₆)alkyl, hydroxy, alkoxy, or alkylthio-~~
 substituted (C₁-C₆)alkyl; and

R^3 and R^4 ~~independently are~~ is ~~hydrogen, a conjugate, (C₁-C₄)alkyl, hydroxy or~~
~~alkoxy or alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio or amino;~~

D and D_m ~~independently are~~ $(CR^6R^7)_z$;

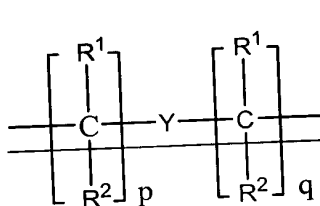
y is 1 and z is 2; each of y and z is zero or an integer from 1 to 10, wherein the sum y
+ z is greater than 2 but not more than 10;

G_m is ~~independently -NR³CO-, -NR³CS-, -NR³SO-, or~~
~~-NR³SO₂- in either orientation;~~

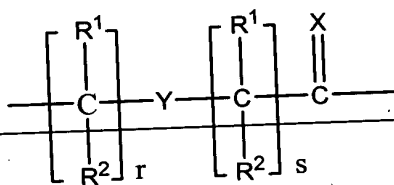
each pair of A-A_m and B-B_m are >N-C(O)-CH₂- ~~selected such that:~~

~~(a) A or A_m is a group of formula (IIa), (IIb) or (IIc) and B or B_m is N or R³N⁺; or~~

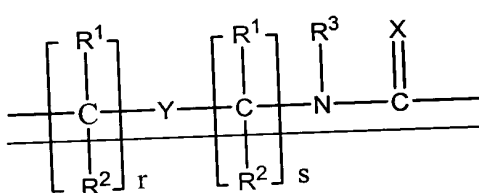
~~(b) A or A_m is a group of formula (IIa) and B or B_m is CH₂;~~



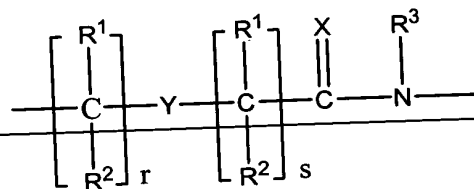
IIa



IIb



IIc



IIId

where:

~~X is O, S, Se, NR³, CH₂ or C(CH₃)₂;~~

~~Y is a single bond, O, S or NR⁴;~~

~~each of p and q is zero or an integer from 1 to 5;~~

~~each of r and s is zero or an integer from 1 to 5;~~

~~_____ R¹ and R² independently are hydrogen, (C₁-C₄)alkyl, hydroxy-substituted (C₁-C₄)alkyl, alkoxy-substituted (C₁-C₄)alkyl, alkylthio-substituted (C₁-C₄)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;~~

I is -NR⁸R⁹ or -NR¹⁰C(O)R¹¹; wherein:

R⁸, R⁹, R¹⁰ and R¹¹ independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer ~~or a conjugate, a reporter enzyme, a reporter molecule, a terpene, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a porphyrin, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and~~

Q is -CO₂H, -CO₂R⁸, -CO₂R⁹, -CONR⁸R⁹, ~~-SO₃H, -SO₂NR¹⁰R¹¹ or an activated derivative of -CO₂H or -SO₃H; and~~

wherein:

~~_____ at least one of Q and I comprises a conjugate selected from a terpene, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or~~

~~_____ at least one of A, A_m, L, and L_m comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;~~

~~_____ wherein said conjugate optionally includes a linking moiety.~~

54-62 (canceled)

63. (new). The peptide nucleic acid of claim 53 wherein R⁸, R⁹, R¹⁰ and R¹¹ independently are hydrogen, alkyl, a peptide, a protein, a carbohydrate, a nucleoside, a

DOCKET NO.: ISIS-1158
Application No.: 08/319,411
Office Action Dated: January 22, 2004

PATENT

nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, or an oligonucleoside.

64. (new). The peptide nucleic acid of claim 53 wherein R^8 , R^9 , R^{10} and R^{11} independently are a nucleoside, a nucleotide, an oligonucleotide, or an oligonucleoside.